UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,973	11/18/2005	Toshio Kitamura	14875- 142US1	5916

26161 7590 12/06/2007
FISH & RICHARDSON PC
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
OUSPENSKI, ILIA I	
ART UNIT	**PAPER NUMBER**
1644	
MAIL DATE	**DELIVERY MODE**
12/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,973	KITAMURA ET AL.	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *3,7 and 9-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-6 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 April 2005* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/10/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence alignment, 6 pages*.

DETAILED ACTION

1. Applicant's remarks, filed on 09/26/2007, are acknowledged.

Claims 1 – 13 are pending.

2. Applicant's election without traverse of Group I (claims 1 – 2, 4 – 6, and 8, drawn to a DNA molecule encoding a protein of SEQ ID NO:2, or comprising the coding region of SEQ ID NO:1; a vector and host cell comprising said DNA, and a method for producing said protein) in the reply filed on 09/26/2007 is acknowledged.

Claims 3, 7, and 9 – 13 are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim.

Claims 1 – 2, 4 – 6, and 8 are presently under consideration, as they read on the elected invention of a DNA encoding SEQ ID NO:2, or comprising SEQ ID NO:1.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reasons set forth herein.

Upon review of the instant application, it is noted that the sequences disclosed at least in Figures 1 and 2 *are not accompanied by SEQ ID Numbers.* Applicant is reminded of the sequence rules which require a submission for all sequences of more than 9 nucleotides or 3 amino acids (see 37 CFR 1.821-1.825) and is also requested to carefully review the submitted specification for any and all sequences which require compliance with the rules. Applicant is reminded to amend the specification and the claims accordingly.

Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) in response to this Office Action.

The SEQ ID Numbers for a sequence shown in a drawing may be incorporated in the Brief Description of the drawing.

4. Receipt is acknowledged of foreign priority papers submitted under 35 U.S.C. 119(a)-(d), which papers are of record in the file of the instant application.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

6. Claims 1 – 2, 4 – 6, and 8 are objected to as reading on non-elected embodiments of the invention, which are not under consideration in the instant application, such as SEQ ID NOS: 3 and 4. Applicant is required to cancel the non-elected embodiments.

7. **35 U.S.C. § 101** reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

8. Claims 1 – 2, 4 – 5, and 8 are rejected under **35 U.S.C. 101** because claimed invention is directed to non-statutory subject matter.

The claims, as presently recited, do not sufficiently distinguish over polypeptides as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products.

The claims are drawn to "a DNA" comprising or encoding the recited sequence. As such, the claims read on naturally occurring murine DNA within native murine chromosomes. "A vector" thus reads on a native chromosome, and "a host cell" reads on a native murine cells within an organism.

In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980). Amending the claims to recite an "isolated" or "recombinant" DNA molecule, vector, and host cell would be remedial in overcoming this rejection. See MPEP 2105.

9. The following is a quotation of the **first paragraph of 35 U.S.C. 112**:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1 – 2, 4 – 6, and 8 are rejected under **35 U.S.C. 112, first paragraph**, because the specification, while being enabling for a DNA molecule encoding a protein consisting of the amino acid sequence of SEQ ID NO:2, or comprising the coding region of the nucleotide sequence of SEQ ID NO:1, does not reasonably provide enablement for:

a DNA encoding a protein comprising am amino acid sequence in which one or more amino acids in the sequence of SEQ ID NO:2 have been replaced, deleted, inserted, and/or added;

a DNA capable of hybridizing with a DNA comprising the nucleotide sequence of SEQ ID NO:1 under stringent conditions; or

a polynucleotide comprising at least 15 nucleotides that is complementary to a DNA comprising the nucleotide sequence of SEQ ID NO:1.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not enable one of skill in the art to make and use the invention as claimed without undue experimentation. Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The claims recite a genus of DNA sequences encoding a protein with an unlimited number of amino acid differences from the reference sequence, i.e. encompassing any sequence whatsoever. The hybridization language also allows for a great degree of sequence variation. Applicant has disclosed a single MC-PIR1 cDNA of SEQ ID NO:1, encoding the predicted amino acid sequence of SEQ ID NO:2, and thus has disclosed only a single member within the claimed genus. In the absence of a particular testable function and some structural basis for that function that must be maintained by the members of the genus, the claimed invention is not described in such a way as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental

research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

Further, even single amino acid differences can result in drastically altered functions of costimulatory proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

In view of this unpredictability, the skilled artisan would not reasonably expect a generically recited polypeptide having at least 80% identity SEQ ID NO:2 to share the same function as the polypeptide of SEQ ID NO:6, and there is insufficient guidance to direct the skilled artisan to such functional sequences. Thus the recitation of percent identity language does not allow the skilled artisan to make and use the encoding nucleic acids commensurate in scope with the instant claims without undue experimentation.

The instant claim language also encompasses polynucleotides comprising at least 15 nucleotides complementary to the recited sequence. Further, the term "comprising" is open ended and extends the nucleic acid molecule to include additional non-disclosed sequences on either or both sides of the disclosed region. As the term "comprising" is applied to sequences other than full length SEQ ID NO:1, or the complete coding region of SEQ ID NO:1, there does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make and use the various fragments encompassed by the instant claims. A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. Without detailed

direction as to which nucleic acid sequences are essential to the function of the encoded polypeptide, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of polypeptide sequences encompassed by the instant claims would share the function of SEQ ID NO:2.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. See In re Fisher, 166 USPQ 18 24 (CCPA 1970). Without sufficient guidance, the structural features of the claimed DNA molecules are unpredictable; thus the experimentation left to those skilled in the art, is unnecessarily, and improperly, extensive and undue.

11. Claims 1 and 2 rejected under **35 U.S.C. 112, first paragraph**, because the specification, while being enabling for a DNA molecule encoding a protein consisting of the amino acid sequence of SEQ ID NO:2, or comprising the coding region of the nucleotide sequence of SEQ ID NO:1, wherein the encoded protein is capable of binding to SHP-1, SHP-2, or SHIP, does not reasonably provide enablement for the claimed DNA molecule wherein the encoded protein is capable of binding DAP10, DAP12, or FcRγ. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant specification discloses at page 2, lines 9 – 15, that the MC-PIR1 protein (SEQ ID NO:2) is capable of binding SHP-1, SHP-2, and SHIP, but not DAP10, DAP12, or FcRγ. Therefore, based on the guidance provided in the specification as-filed, one of skill in the art is not enabled to make and use DNA molecules within the scope of the claims which encode a protein capable of binding to DAP10, DAP12, or FcRγ.

12. Claims 1 – 2, 4 – 6, and 8 are rejected under **35 U.S.C. 112, first paragraph**, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant is not in possession of:

a DNA encoding a protein comprising am amino acid sequence in which one or more amino acids in the sequence of SEQ ID NO:2 have been replaced, deleted, inserted, and/or added;

a DNA capable of hybridizing with a DNA comprising the nucleotide sequence of SEQ ID NO:1 under stringent conditions; or

a polynucleotide comprising at least 15 nucleotides that is complementary to a DNA comprising the nucleotide sequence of SEQ ID NO:1.

The claims recite a genus of DNA sequences encoding a protein with an unlimited number of amino acid differences from the reference sequence, i.e. encompassing any sequence whatsoever. The hybridization language also allows for a great degree of sequence variation. Applicant has disclosed a single MC-PIR1 cDNA of SEQ ID NO:1, encoding the predicted amino acid sequence of SEQ ID NO:2, and thus has disclosed only a single member within the claimed genus; therefore, the skilled artisan cannot envision all the contemplated sequence possibilities encompassed by the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has

occurred, regardless of the complexity or simplicity of the invention. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

In the absence of sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, the claimed invention is not described in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The instant claim language also encompasses polynucleotides comprising at least 15 nucleotides complementary to the recited sequence. Further, the term "comprising" is open ended and extends the nucleic acid molecule to include additional non-disclosed sequences on either or both sides of the disclosed region. As the term "comprising" is applied to sequences other than full length SEQ ID NO:1, or the complete coding region of SEQ ID NO:1, there does not appear to be sufficient written description in the specification as filed to convey to the skilled artisan that the inventors, at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, January 5, 2001.

13. The following is a quotation of the appropriate paragraphs of **35 U.S.C. 102** that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1 – 2, 4 – 5, and 8 are rejected under **35 U.S.C. 102(b)** as being anticipated by GenBank entry of Accession Number AK045869 (1999, of record – cited in the previous Office Action; see entire document).

GenBank entry of Accession number AK045869 teaches a cDNA sequence which is 96.2% identical to the instantly recited SEQ ID NO:1, as evidenced by the attached alignment. As such, the sequence of AK045869 is capable of hybridizing with DNA of SEQ ID NO:1 under stringent conditions, and therefore anticipates the instant claim 1. Since the nucleic acid taught by the reference is structurally the same as instantly claimed, it inherently possess the same functional properties, including the ability of the encoded protein to interact with the proteins recited in claim 2. Furthermore, since the reference teaches a cDNA obtained as a result of molecular cloning, which involves creating a cDNA library in a vector in bacterial host cells, both a vector and a host cell are inherently taught by the reference.

Therefore, the reference teachings anticipate the instant claimed invention.

15. The following is a quotation of **35 U.S.C. 103(a)** which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1, 5, and 6 rejected under **35 U.S.C. 103(a)** as being obvious over GenBank entry of Accession Number AK045869 (1999, of record – cited in the previous Office Action; see entire document).

The reference of GenBank entry of Accession number AK045869 has been discussed supra, and teaches a nucleic acid within the scope of the instant claim 1, as well as a vector and host cell comprising said nucleic acid.

The reference does not explicitly teach a method of producing a protein encoded by the nucleic acid.

However, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to produce the protein encoded by the nucleic acid. The cDNA clone taught by the reference was obtained as the result of a large-scale genomic research effort, and as one of skill in the art is aware, it is generally desirable to complement such projects by proteomics analysis, which involves expressing the proteins encoded by identified cDNA clones. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to express the protein. The skilled artisan would have a reasonable expectation of success in doing so, because the methods involved were routine in the art at the time the invention was made.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

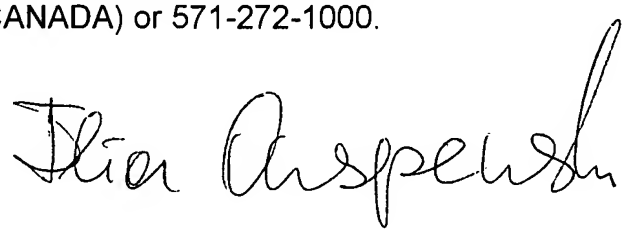
17. Conclusion: no claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ILIA OUSPENSKI, Ph.D.
Patent Examiner
Art Unit 1644



December 3, 2007